REMARKS

Claims 1, 2, 4-35, 37, 38, and 40-42 are currently pending. With entry of the instant amendment, claims 2, 34, 41, and 42 have been amended. The amendments to the claims add no new matter and are fully supported by the application as filed.

For convenience, the rejections are addressed in the order presented in the Office Action mailed April 17, 2003.

Rejections under 35 U.S.C. § 101, utility--claims 37, 38, and 40

Claims 37, 38, and 40 were rejected as allegedly lacking utility. The rejection alleges that there is no specific or well-established utility for inhibiting the growth of HIV in a cell *in vitro* by transducing the cells with the claimed vectors. Specifically, the examiner alleges that the only readily apparent use of the claimed method is to study the effects of the method. Applicants respectfully traverse.

The application asserts a specific, substantial and credible utility that is beyond studying the effects of the methods themselves For example, on page 7, lines 12-15, the specification states that the vectors of the invention can be used to inhibit the infection, replication or spread of a virus, *e.g.,* HIV, in a population of cells, such as a cell culture or cell isolate. Moreover, examples presented in the specification disclose that constructs of the invention successfully inhibit HIV growth in T cells (*see, e.g.,* page 47, line 26 though page 48, line 7). The Examiner provides no evidence or reasoning as to why this utility is not credible, substantial or specific.

First, a "specific utility" is specific to the subject matter claimed (MPEP §2107.01(I)(A)). Applicants have disclosed a viral vector system that can be used for the inhibition of viral replication *in vitro*. The claimed invention is specific to this subject matter. Therefore, the specificity aspect of the utility requirement is met.

Second, a utility must be "substantial", *i.e.,* it defines a real world use. Inhibition of viral replication in an *in vitro* setting is a method of controlling virus levels in a cell population and can also be used to prevent the spread of a virus *in vitro*. This is a real-world

context of use. The Examiner provides no evidence to the contrary. Thus, the claims meet the second aspect of the utility requirement.

Lastly, the utility is credible. As assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (b) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (MPEP §2107.02(III)(B)). The Examiner must determine if the assertion of utility is believable to a person of ordinary skill in the art (*see, e.g.,* MPEP § 2107.02IIIB) and provide evidence to support an assertion that the utility is not credible (MPEP § 2107.02IV). Applicants have shown that the method inhibits HIV replication *in vitro*, which can limit the spread of the virus in a cell population. No evidence has been provided by the Examiner to support the position that one of skill in the art would not find this to be a credible utility.

In addition, in some embodiments, cells transduced by the vectors *in vitro* can further be used in a patient (*see, e.g.,* page 30, line 30 through page 31, line 11), *e.g.,* to limit HIV infection or spread. Thus, the method also has use as a method for limiting virus spread or infection in *ex vivo* procedures in which cells are manipulated outside of the patient and re-introduced into the patient (*e.g.,* lymphocyte infusions, transplants).

As explained above, the invention claimed in claims 37, 38, and 40 meet the utility requirements for patentability. Accordingly, one of skill would also know how to use the invention. Applicants therefore respectfully request withdrawal of the utility rejection and rejection under 35 U.S.C. 112, first paragraph.

Rejection of claims 41 and 42

Claims 41 and 42 were rejected as allegedly lacking utility because the claims are directed to non-statutory subject matter. The Examiner argues that the claims encompass a cell contained within human beings, which is not patentable subject matter. Claims 41 and 42 have been amended to recite "an isolated cell". Applicants therefore respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 2 and 42 were rejected as allegedly indefinite with regard to the recitation of a "vector nucleic acid that further encodes and HIV Rev binding subsequence" and "selected from the group of cells comprising", respectively. Claim 34 was recited for insufficient antecedent bases for the term "the dicistronic mRNA."

Claim 2 has been amended to delete the phrase noted by the Examiner; claim 42 has been amended to recite "consisting of" rather than "comprising", and claim 34 has been amended to substitute the term "the multicistronic" for "the dicistronic." Applicants therefore request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, first paragraph--enablement

Claims 1, 2, 4-35, 41 and 42 were rejected as allegedly not enabled. The Examiner alleges that the claims are not enabled because the claims read on gene therapy *in vivo*. In particular, the Examiner appears to believe that the sole uses of the vectors are as gene therapy vectors and that the claims are therefore not enabled. Applicants respectfully traverse. The claims at issue are composition claims, not claims to methods of performing gene therapy *in vivo*. The arguments presented in the Office Action do not properly address the enablement of the composition claims.

The claimed compositions are transduction vectors for introducing genes into a cell. Expression of the introduced genes, viral inhibitor sequences, can further be controlled by rev sequences that are introduced into the cell after transduction with the vector or that are expressed in the cell at the time of transduction. Cell transduction can be performed either *in vitro* or *in vivo*, as plainly recited in the specification. For example, in an *in vitro* use, the transduction vectors of the invention are used to limit the growth of a virus in a population of cells. Thus, the cell transduction in vector are useful for applications in which it is desirable to control virus levels in a population of cells. These compositions are fully enabled by the specification.

Applicants have taught how to make the vectors. The individual components of the vector are well known in the art. The specification provides guidance as to how to select the

components and incorporate them into the vectors. For example, on page 27, beginning at line 26, Applicants directs the practitioner regarding the selection of promoters. On page 28, beginning at line 17, Applicants teach the construction of multicistronic vectors, including the incorporation of such elements as IRES. Applicants also teach the positioning of the inhibitor and the other sequences (*see, e.g.,* Figure 5).

Applicants have also taught how to use the vectors. For example, the specification describes cellular transformation (*e.g.,* page 30) and includes examples showing that the vectors successfully transduce cells and limit viral replication (*see, e.g.,* pages 47 and 48).

Thus, Applicants have taught how to make and use the invention and have thereby enabled the claims. As noted above, the Examiner's arguments are directed to *in vivo* methods of gene therapy and the use of the vectors. The Examiner is reminded that Applicants need only made one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. § 101 and 35 U.S.C. § 112 (MPEP § 2107.02(I)). Applicants have met this requirement: the specification demonstrates that these vectors can be used as transduction vectors *in vitro* in addition to describing their use *in vivo*.

The Examiner also alleges that claim 18, which recites a pharmaceutical excipient, specifically implies an *in vivo* therapeutic use. Again, the vector can also be used with a pharmaceutical excipient, for transducing cells *in vitro*. Thus, claim 18 is also not limited to the context of a method of performing gene therapy *in vivo*.

Lastly, the Examiner alleges that the specification fails to provide adequate guidance for identifying splice donor and acceptor subsequences for use in the invention. Specifically, the Examiner argues that the term "subsequence" in this context means that the splice donor and acceptor sites could include smaller regions than the consensus donor and acceptor sequences. However, the specification clearly teaches that the splice donor and acceptor sites, *i.e.,* the SD and SA subsequences contained within the vectors of the invention, are functional (*see, e.g.,* page 16, lines 2-7). Thus, the SD and SA subsequences must have the regions that are essential for activity. The Examiner presents no reasoning or evidence as to why

the practitioner would not understand that the SD and SA sites in the vector function, and include the structural features required for activity.

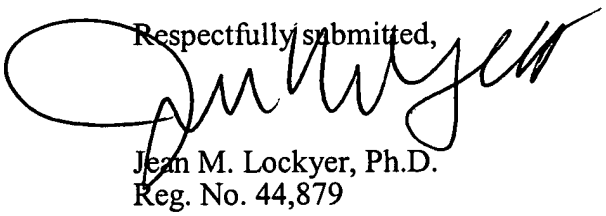
In view of the foregoing, the claims are properly enabled. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Jean M. Lockyer, Ph.D.
Reg. No. 44,879

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
JML:jml
SF 1477722 v1